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A General Synthesis of Phosphonic Acid Dichlorides using Oxalyl Chloride and DMF Catalysis

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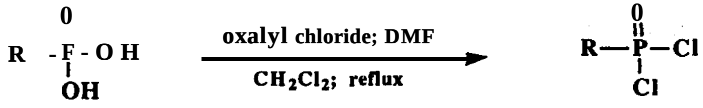
Abstract: A general synthesis of phosphonic diacid dichlorides (1) using oxalyl chloride and catalytic DMF is described.

There are scattered reports in the literature of the synthesis of phosphorous acid chlorides. Those which start from alkylphosphonic diesters use phosphorous pentachloride [1a, 1b] or thionyl chloride2 as the halogenating agent. However, phosphorous oxychloride and ethyl or methylchloride are troublesome side products generated under these conditions, and these reactions suffer from variable yields. Other procedures[3a, 3b] first converted phosphorous alkyl diesters into silyl diesters before reaction with phosphorous pentachloride or oxalyl chloride. In addition to the extra chemical transformation required. one now has a volatile silyl chloride as a side product, which is problematic on large scale. A third approach has been the direct halogenation of phosphonic acids to phosphonic dichlorides. Again, phosphorous pentachloride[4 - 6] has been widely used, but again, the yields are mixed. Also, in all cases, one must distill the phosphonic dichloride product. Herein is reported an efficient and broadly applicable method for generating phosphonic acid dichlorides (1) on large scale without distillation.

Scheme



$$\mathrm{R-\overset{O}{\underset{OH}{P}}-OH} \xrightarrow[\mathrm{CH_2Cl_2;\ reflux}]{\text{oxalyl chloride; DMF}} \mathrm{R-\overset{O}{\underset{Cl}{P}}-Cl}$$

1

While them are few good methods of monitoring the transformation of carboxylic acids to carboxylic acid chlorides apart from derivitization and analysis. one can accurately follow the conversion of phosphonic acids to phosphonic acid dichlorides by ^{31}P nmr. Typically, the ^{31}P signal is shifted 14 to 20 ppm upfield (see Table), simplifying analysis.

The phosphonic acid starting materials were either obtained from commercial sources or prepared via Arbuzov chemistry6 followed by acid hydrolysis. The DMF-catalyzed reaction of a phosphonic diacid with oxalyl chloride is strongly endothermic and liberates large quantities of gas, as described by the equation:

$$\mathrm{R\text{-}P(O)(OH)_2 + 2\ ClC(O)C(O)Cl \longrightarrow R\text{-}P(O)(Cl)_2 + 2HCl + 2C0 + 2CO_2}$$

Distillation of the crude acid chlorides was not required, but is possible via vacuum distillation. For undistilled acid dichlorides, yields were generally >93%, while distilled yields, when performed for comparison to reported values,[8] were in the range of 85 - 92%. All reagents were obtained from commercial sources and used without further purification, and all ^{31}P nmrs were recorded at 80.99 MHz on a Varian VXR 200 without internal standard in $CDCl_3$.

Table

	$R\text{-}P(O)Cl_2$					
	yield, %		b.p., °C (mm Hg)		^{31}P nmr peak, ppm	
R	crude	distilled	found	lit.[8]	$RP(O)Cl_2$	$RP(O)(OH)_2$
C_6H_{11}-	94	92	178 (21)	127 (15)	59.6	40.9
C_6H_{11}-CH_2-	95	NA	NA	---	50.8	32.2
C_6H_{11}-$(CH_2)_4$-	94	NA	NA	---	52.6	32.0
CH_2=$CHCH_2$-	92	85	127 (8)	77 (5)	33.1	19.2
C_6H_5-	93	89	107 (4)	105 (4)	37.3	20.9
C_6H_5-CH=$CHCH_2$-	91	NA	NA	—	47.4	23.7

Typical is the synthesis of phenylphosphonic dichloride. A solution of phenylphosphonic acid (2.0 G) and anhydrous DMF (10 μL) was **gently refluxed** in dichloromethane (30 mL) under dry nitrogen. To this, a solution of oxalyl chloride (2.4 mL) in anhydrous dichloromethane was added, via modified addition funnel.7 During the addition, copious gas was evolved, and heat was applied to keep the reaction temperature at or above 35° C. Upon complete addition of the oxalyl chloride solution, the reaction was held at reflux for approximately one hour, then the reflux condenser was replaced by a still head, and the volatiles (distillation temperature < 70° C at 763 mm) were removed. Analysis of the residual brown oil (2.29 G; 93%) by ^{31}P nmr revealed a single peak (see Table), consistent with clean formation of phenylphosphonic dichloride. The product was distilled only for comparison to the literature value.* and could be used without distillation.

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7. A pressure-equalizing addition funnel's drip tube was extended with teflon tuhing **such that it reached below the surface of the reaction solution.**
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